Natrapharm

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Pregabalin + Methylcobalamin

Nervagest® Plus

75 mg / 750 mcg Capsule
Antiepileptic / Vitamin
(Cyanocobalamin analogue)

Formulation:
Each hard gelatin capsule contains:
Pregabalin, BP 75mg
Methylcobalamin, USP .... 750 mcg

Product Description:
Size 4, Red cap and Body Hard gelatin capsule containing pale pink colored powder.

Pharmaceutical Form:
Nervagest® Plus (75mg/750mcg) Capsule

Pharmacotherapeutic group: other anti-epileptics with B12 Cyanocobalamin analogue (Methylcobalamin)
ATC-Code: N03AX16 with B03BA05
Pharmacodynamic effects
Pregabalin
Pregabalin is a structural derivative of the inhibitory neurotransmitter, gamma-aminobutyric acid (GABA). Pregabalin does not bind directly to $GABA_A$, $GABA_B$, or benzodiazepine receptors, does not augment $GABA_A$ responses in cultured neurons, does not alter rat brain GABA concentration or have acute effects on GABA uptake or degradation. However, in cultured neurons, prolonged application of pregabalin increases the density of GABA transporter protein and increases the rate of functional GABA
transport. Pregabalin binds with high affinity to the $alpha_2$-delta site (an auxiliary submit of voltage-gated calcium channels) in central nervous system tissues. Although the mechanism of action of pregabalin is unknown, results with genetically modified mice and with compounds structurally related to pregabalin (such as gabapentin) suggest that binding to the $alpha_2$-delta submit may be involved in pregabalin's antinociceptive and antiseizure effects in animal models. In vitro, pregabalin reduces the calcium dependent release of several neurotransmitters, possibly by modulation of calcium channel function. Pregabalin does not block sodium channels, is not active at opiate receptors, and does not alter cyclooxygenase enzyme activity. It is inactive at serotonin and dopamine receptors and does not inhibit dopamine, serotonin, or noradrenaline reuptake.

Methylcobalamin
Methylcobalamin (Mecobalamin, MeCbl), is one of the two biologically active vitamin B12. Mecobalamin acts as an important cofactor in the reaction of one class of the B12 enzymes, the methyltransferases. The B12-dependent methyltransferases play an important role in amino acid metabolism in many organisms as well as in one-carbon metabolism and Co_2 fixation in anaerobic microbes. Among them, methionine synthase is the most extensively studied B12-dependent methyltransferase in humans. As the cofactor of the enzyme methionine synthase, mecobalamin functions to catalyse the transfer of the methyl group from methylene tetrahydrofolate to homocysteine (Hcy) to form methionine and tetrahydrofolate. Because mecobalamin acts as an important cofactor of methionine synthesis, supplements of mecobalamin enhance the efficiency of the remethylation pathway, consequently accelerating Hcy consumption and reducing its concentration. Thus, lowering homocysteine concentrations to the normal range (4 - 15 µmol/l) seems to be an effective therapeutic method in decreasing the risks of the diseases mentioned above.

Pharmacokinetic properties
Pregabalin
Absorption: Pregabalin oral bioavailability is ≥ 90% and is independent of dose. Following single - (25 to 300 mg) and multiple- dose (75 to 900 mg/day) administration, maximum plasma concentrations (C_{max},) and area under the plasma concentration-time curve (AUC) values increase linearly. Following repeated administration, steady state is achieved within 24 to 48 hours.

Distribution
Pregabalin does not bind to plasma proteins. The apparent volume of distribution of pregabalin following oral administration is approximately 0.5 L/kg.

Elimination
Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug with a mean elimination half-life of 6.3 hours in subjects with normal renal function. Mean renal clearance was estimated to be 67.0 to 80.9 mL/min in young healthy subjects.

Methylcobalamin
Absorption
Evidence indicates methylcobalamin is utilized more efficiently than cyanocobalamin to increase levels of one of the coenzyme forms of vitamin B12. Experiments have demonstrated similar absorption of methylcoblamin following oral administration. The quantity of cobalamin detected following a small oral dose of mecobalamin is similar to the amount detected following the administration of cyanocobalamin, but significantly more cobalamin accumulates in liver tissue, which is associated with mecobalamin intake.
Distribution and Metabolism
Cobalamin circulates in plasma bound to two carrier proteins: transcobalamin (TC) and haptocorrin. TC is a 43-kDa non-glycoprotein that transfers cobalamin from the intestine into the blood stream and then into all the cells of the body. Cobalamin-saturated transcobalamin (holoTC) constitutes 6 - 20% of total plasma cobalamin. The unsaturated TC is called apotranscobalamin, which constitutes the major part of TC. Additionally, total homocysteine (tHcy) and methylmalonic acid are considered to be two functional markers of vitamin B12 status in adults.
Excretion: Human urinary excretion of methylcobalamin is about one third that of a similar dose of cyanocobalamin, indicating substantially greater tissue retention.

Indication: Nervagest® Plus Capsule is indicated for Management of neuropathic pain associated with peripheral neuropathy. Adjunct therapy for adult patient with partial onset of seizures. Management of Neuralgia. Management of Fibromyalgia.

Dosage and Administration:
Starting Dose: 1 cap twice daily; provided this is tolerable vis-a-vis renal function. Patients previously on gabapentin will have a wash-out period of 1 week prior to start of dosing with pregabalin.

Special populations
Renal impairment and haemodialysis
Pregabalin clearance is nearly proportional to creatinine clearance (CrCl). Dosage reduction in patients with renal dysfunction is necessary. Pregabalin is effectively removed from plasma by haemodialysis. Following a 4-hour haemodialysis treatment, plasma pregabalin concentrations are reduced by approximately 50%. For patients on haemodialysis, dosing must be modified.
Paediatric Pharmacokinetics
Pharmacokinetics of pregabalin has not been adequately studied in paediatric patients.

Contraindications: Nervagest® Plus is contraindicated in patients who are hypersensitive to pregabalin or methylcobalamin or any of the components of this product.

Warnings and precautions
General
Angioedema
There have been post marketing reports of angioedema in patients during initial and chronic treatment with pregabalin. Specific symptoms included swelling of the face, mouth (tongue, lips, and gums), and neck (throat and larynx). There were reports of life threatening angioedema with respiratory compromise requiring emergency treatment. Pregabalin should be discontinued immediately in patients with these symptoms. Caution should be exercised when prescribing pregabalin to patients who have had a previous episode of angioedema. In addition, patients who are taking other drugs associated with angioedema (e.g., angiotensin converting enzyme inhibitors) may be at increased risk of developing angioedema.
Hypersensitivity
There have been post marketing reports of hypersensitivity in patients shortly after initiation of treatment with pregabalin. Undesirable effects included skin redness, blisters, hives, rash, dyspnea, and wheezing. Pregabalin should be discontinued immediately in patients with these symptoms.
Suicidal behavior and ideation
Antiepileptic drugs (AEDs), induding pregabalin, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Anyone considering prescribing pregabalin or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Should suicidal thoughts and behavior emerge during treatment, the prescriber needs to consider whether the emergence of these symptoms in any given patient may be related to the illness being treated Patients, their caregivers, and families should be informed that AEDs increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of the signs and symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers.
Tumorigenic Potential
In standard preclinical in vivo lifetime carcinogenicity studies of pregabalin, an unexpectedly high incidence of hemangiosarcoma was identified in two different strains of mice. The clinical significance of this finding is unknown. Clinical experience during pregabalin's premarketing development provides no direct means to assess its potential for inducing tumors in humans. In clinical studies across various patient populations, comprising 6396 patient-years of exposure in patients >12 years of age, new or worsening-preexisting tumors were reported in 57 patients. Without knowledge of the background incidence and recurrence in similar populations not treated with pregabalin, it is impossible to know whether the incidence seen in these cohorts is or is not affected by treatment.
Treatment of central neuropathic pain due to spinal cord injury
In the treatment of central neuropathic pain due to spinal cord injury the incidence of adverse reactions in general, central nervous system adverse reactions and especially somnolence was increased. This may be attributed to an additive effect due to concomitant medicinal products (e.g. anti-spasticity agents) needed for this condition. This should be considered when prescribing pregabalin in this condition.
Dizziness and Somnolence
Pregabalin may cause dizziness and somnolence. Patients should be informed that pregabalin-related dizziness and somnolence may impair their ability to perform tasks such as driving or operating machinery.
In the pregabalin controlled trials, dizziness was experienced by 30% of pregabalin • treated patients compared to 8% of placebo-treated patients; somnolence was experienced by 23% of pregabalin • treated patients compared to 8% of placebo-treated patients. Dizziness and somnolence generally began shortly after the initiation of pregabalin therapy and occurred more frequently at higher doses. Dizziness and somnolence were the undesirable effects most frequently leading to withdrawal from controlled studies. In pregabalin • treated patients reporting these undesirable effects in short-term, controlled studies, dizziness persisted until the last dose in 30% and somnolence persisted until the last dose in 42% of patients.
Ophthalmological Effects
In controlled studies, a higher proportion of patients treated with pregabalin reported ophthalmological effects like blurred vision, reduction in visual acuity and changes in visual field and fundoscopy. Although the clinical significance of the ophthalmologic findings is unknown, patients should be informed that if changes in vision occur, they should notify their physician. If visual disturbance persists, further assessment should be considered. More frequent assessment should be considered for patients who are already routinely monitored for ocular conditions.
Reduced lower gastrointestinal tract function
There are post-marketing reports of events related to reduced lower gastrointestinal tract function (e.g., intestinal obstruction, paralytic ileus, constipation) when pregabalin was co-administered with medications that have the potential to produce constipation, such as opioid analgesics. When pregabalin and opioids will be used in combination, measures to prevent constipation may be considered (especially in female patients and elderly).
Abuse potential Cases of abuse have been reported. Caution should be exercised in patients with a history of substance abuse and the patient should be monitored for symptoms of pregabalin abuse.
Encephalopathy Cases of encephalopathy have been reported, mostly in patients with underlying conditions that may precipitate encephalopathy.
Withdrawal symptoms
After discontinuation of short-term and long-term treatment with pregabalin withdrawal symptoms have been observed in some patients. The following events have been mentioned: insomnia, headache, nausea, anxiety, diarrhoea, flu syndrome, nervousness, depression, pain, convulsion, hyperhidrosis and dizziness. The patient should be informed about this at the start of the treatment. Convulsions, including status epilepticus and grand mal convulsions, may occur during pregabalin use or shortly after discontinuing pregabalin. Concerning discontinuation of long-term treatment of pregabalin there are no data of the incidence and severity of withdrawal symptoms in relation to duration of use and dose of pregabalin.
Weight Gain
Pregabalin treatment may cause weight gain. In pregabalin controlled clinical trials, pregabalin associated weight gain was related to dose and duration of exposure, but did not appear to be associated with baseline BMI, gender, or age. Weight gain was not limited to patients with edema. Although weight gain was not associated with clinically important changes in blood pressure in short-term controlled studies, the long-term cardiovascular effects of pregabalin-associated weight gain are unknown.
Among diabetic patients, pregabalin was associated with higher weight gain as compared to placebo treated patients. However, the effects of this pregabalin-associated weight gain on glycemic control have not been systematically assessed. In controlled and longer-term open label clinical trials with diabetic patients, pregabalin treatment did not appear to be associated with loss of glycemic control (as measured by HbA_{1c})-
Dermatopathy
Diabetic patients should be instructed to pay particular attention to skin integrity while being treated with pregabalin. Some animals treated with pregabalin developed skin ulcerations, although no increased incidence of skin lesions associated with pregabalin was observed in clinical trials.
Male fertility
Men being treated with pregabalin whoa plan to father a child should be informed of the potential risk of male-mediated teratogenicity. In preclinical studies in rats, pregabalin was associated with an increased risk of male-mediated teratogenicity. The clinical significance of this finding is uncertain.
Peripheral Edema
Pregabalin treatment may cause edema, primarily described as peripheral edema. In short- term trials of patients without clinically significant heart or peripheral vascular disease, there was no apparent association between peripheral edema and cardiovascular complications such as hypertension or congestive heart failure. Peripheral edema was not associated with laboratory changes suggestive of deterioration in renal or hepatic function. Higher frequencies of weight gain and peripheral edema were observed in patients taking both pregabalin and a thiazolidinedione antidiabetic agent compared to patients taking either drug alone. As the thiazolidinedione class of antidiabetic drugs can cause weight gain and/or fluid retention, possibly exacerbating or leading to heart failure, care should be taken when co-administering pregabalin and these agents. Because there are limited data on congestive heart failure patients with New York Heart Association (NYHA) Class III or IV cardiac status, pregabalin should be used with caution in these patients.
Creatine Kinase Elevations
Pregabalin treatment was associated with creatine kinase elevations as compared to placebo in controlled clinical trials. The relationship between these myopathy events and pregabalin is not completely understood because the cases had documented factors that may have caused or contributed to these events. Patients should be instructed to promptly report unexplained muscle pain, tenderness, or weakness, particularly if these muscle symptoms are accompanied by malaise or fever. Pregabalin treatment should be discontinued if myopathy is diagnosed or suspected or if markedly elevated creatine kinase levels occur.
Decreased Platelet Count
Pregabalin treatment was associated with a decrease in platelet count. Pregabalin
related subjects experienced a mean maxima decrease in platelet count of 20 x 10^3/µL, compared to 11 x 10^3/µL in placebo patients. In the overall database of controlled trials, 2% of placebo patients and 3% of pregabalin patients experienced a potentially clinically significant decrease in platelets, defined as 20% below baseline value and <150 x 10^3/µL. A single pregabalin treated subject developed severe thrombocytopenia with a platelet count less than 20 x 10^3/µL. In randomized controlled trials, pregabalin was not associated with an increase in bleeding-related undesirable effects.
PR Interval Prolongation
Pregabalin treatment was associated with PR interval prolongation. In analyses of clinical trial ECG data, the mean PR interval increase was 3-6 msec at pregabalin doses >/= 300 mg/day. This mean change difference was not associated with an increased risk of PR increase >/= 25% from baseline, an increased percentage of subjects with on-treatment PR >200 msec, or an increased risk of undesirable effects of second or third degree AV block.
Subgroup analyses did not identify an increased risk of PR prolongation in patients with baseline PR prolongation on or in patients taking other PR prolonging medications. However, these analyses cannot be considered definitive because of the limited number of patients in these categories.
Drug abuse and dependence
Pregabalin is a Schedule V controlled substance.
Pregabalin is not known to be active at receptor sites associated with drugs of abuse. As with any CNS active drug, physicians should carefully evaluate patients for history of drug abuse and observe them for signs of pregabalin misuse or abuse (e.g.,development of tolerance, dose escalation, and drug-seeking behavior).
Others
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Interaction with other medicinal products and other forms of interaction
Pregabalin, at concentrations that were, in general, 10-times those attained in clinical trials, does not inhibit human CYP1A2, CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4 enzyme systems. *In vitro* drug interaction studies demonstrate that pregabalin does not induce CYP1A2 or CYP3A4 activity. Therefore, an increase in the metabolism of co-administered CYP1A2 substrates (e.g. theophylline, caffeine) or CYP 3A4 substrates (e.g. midazolam, testosterone) is not anticipated.
The drug interaction studies described below were conducted in healthy adults, and across various patient populations.
Gabapentin Gabapentin pharmacokinetics following single- and multiple-dose administration was unaltered by pregabalin co-administration. The extent of pregabalin absorption was unaffected by gabapentin co-administration, although there was a small reduction in rate of absorption.
Oral Contraceptive Pregabalin co administration (200 mg three times a day) had no effect on the steady-state pharmacokinetics of norethindrone and ethinyl estradiol (1 mg/35 µg, respectively) in healthy subjects.
Lorazepam Multiple-dose administration of pregabalin (300 mg twice a day) in healthy subjects had no effect on the rate and extent of lorazepam single-dose pharmacokinetics and single-dose administration of lorazepam (1 mg) had no effect on the steady-state pharmacokinetics of pregabalin.
Oxycodone Multiple-dose administration of pregabalin (300 mg twice a day) in healthy subjects had no effect on the rate and extent of oxycodone single-dose pharmacokinetics. Single-dose administration of oxycodone (10 mg) had no effect on the steady-state pharmacokinetics of pregabalin.
Ethanol Multiple-dose administration of pregabalin (300 mg twice a day) in healthy subjects had no effect on the rate and extent of ethanol single-dose pharmacokinetics and single-dose administration of ethanol (0.7 g/kg) had no effect on the steady-state pharmacokinetics of pregabalin.
Antiepileptic Drugs
Steady-state trough plasma concentratons of phenytoin, phenobarbital, topiramate, carbamazepine and carbamazepine 10, 11 epoxide, valproic acid, and lamotrigine were not affected by concomitant pregabalin (200 mg three times a day) administration.
These drugs have no effect on the pharmacokinetics of pregabalin and pregabalin has no effect on the pharmacokinetics of the mentioned drugs. Tiagabine also had no effect the pharmacokinetics of pregabalin.
As with all AEDs, pregabalin should be withdrawn gradually to minimize the potential of increased seizure frequency in patients with seizure disorders. If pregabalin is discontinued this should be done gradually over a minimum of 1 week.
Oral hypoglycemic Concomitant administration of glyburide, insulin or metformin with pregabalin did not affect the pharmacokinetics of pregabalin.
Furosemide Concomitant administration of furosemide with pregabalin did not affect the pharmacokinetics of pregabalin.
CNS Depressants Patients who require concomitant treatment with CNS depressants such as opiates or benzodiazepines should be informed that they may experience additive CNS side effects, such as somnolence.
Alcohol Patients should be told to avoid consuming alcohol while taking pregabalin, as pregabalin may potentiate the impairment of motor skills and sedating effects of alcohol.
Antibiotics May alter the intestinal microflora and may decrease the absorption of methylcobalamin.
Cholestyramine, colchicines or colestipol May decrease the enterohepatic re-absorption of methylcobalamin.
Metformin, para-aminosalicylic acid and potassium chloride May decrease the absorption of methylcobalamin.
Nitrous oxide Can produce a functional methylcobalamin deficiency.
Patient with Renal impairment Pregabalin dosage adjustment should be considered in cases of renal impairment. (Refer to Dosage and Administration, Patients with renal impairment)

Drug Interactions
Absorption of vitamin B12 from the gastrointestinal tract may be reduced by neomycin, aminosalicylic acid, histamine H2-antagonists, omeprazole and colchicine. Serum concentrations may be decreased by use of oral contraceptives. Many of these interactions are unlikely to be of clinical significance but should be taken into account when performing assays for blood concentrations. Parenteral chloramphenicol may attenuate the effect of vitamin B12 in anemia.

Pregnancy and lactation
Pregnancy Category C
Increased incidences of fetal structural abnormalities and other manifestations of developmental toxicity, including lethality, growth retardation and nervous and reproductive system functional impairment, were observed in the offspring of rats and rabbits given pregabalin during pregnancy at doses that produced plasma pregabalin exposures (AUC) ≥ 5 times human exposure at the maximum recommended dose of 600 mg/day. There are no adequate and well-controlled studies in pregnant women. Pregabalin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Lactation It is not known if pregabalin is excreted in human milk; it is, however, present in the milk of rats. Because many drugs are excreted in human milk, and because of the potential for tumorigenicity shown for pregabalin in animal studies, a decision
should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
Paediatric use Safety and effectiveness in paediatric patients have not been established.
Undesirable effects The most common side effects events seen with pregabalin treatment are dizziness, somnolence, headache, ataxia, asthenia, dry mouth, constipation, edema, blurred vision, weight gain, and "thinking abnormal" (primarily difficulty with concentration/attention). Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. In all controlled and uncontrolled trials across various patient populations during the premarketing development of pregabalin, more than 10,000 patients have received pregabalin. Approximately 5000 patients were treated for 6 months or more, over 3100 patients were treated for 1 year or longer, and over 1400 patients were treated for at least 2 years.
Controlled Studies with Neuropathic Pain Associated with Diabetic Peripheral Neuropathy
Undesirable Effects Leading to Discontinuation
In clinical trials in patients with neuropathic pain associated with diabetic peripheral neuropathy, 9% of patients treated with pregabalin and 4% of patients treated with placebo discontinued prematurely due to undesirable effects. In the pregabalin treatment group, the most common reasons for discontinuation due to undesirable effects were dizziness (3%) and somnolence (2%). In comparison, <1% of placebo patients withdrew due to dizziness and somnolence. Other reasons for discontinuation from the trials, occurring with greater frequency in the pregabalin group than in the placebo group, were asthenia, confusion, and peripheral edema. Each of these events led to withdrawal in approximately 1% of patients.
Most Common Undesirable Effects
Table 1 lists all undesirable effects, regardless of causality, occurring in ≥1% of patients with neuropathic pain associated with diabetic neuropathy in the combined pregabalin group for which the incidence was greater in this combined pregabalin group than in the placebo group. A majority of pregabalin-treated patients in clinical studies had undesirable effects with a maximum intensity of "mild" or "moderate".
Table 1: Treatment-emergent adverse reaction incidence in controlled trials in Neuropathic Pain Associated with Diabetic Peripheral Neuropathy (Events in at least 1 % of all pregabalin-treated patients and at least numerically more in all pregabalin than in the placebo group)

Body System- preferred term	75mg/day	150mg/day	300mg/day	600mg/day	All PGB*%	Placebo%
Body as a whole						
Asthenia	4	2	4	7	5	2
Accidental injury	5	2	2	6	4	3
Back pain	0	2	1	2	2	0
Chest pain	4	1	1	2	2	1
Face edema	0	1	1	2	1	0
Digestive system						
Dry mouth	3	2	5	7	5	1
Constipation	0	2	4	6	4	2
Flatulence	3	0	2	3	2	1
Metabolic and nutritional disorders						
Peripheral edema	4	6	9	12	9	2
Weight gain	0	4	4	6	4	0
Edema	0	2	4	2	2	0
Hypoglycemia	1	3	2	1	2	1
Nervous system						
Somnolence	4	6	13	16	12	3
Neuropathy	9	2	2	5	4	3
Ataxia	6	1	2	4	3	1
Vertigo	1	2	2	4	3	1
Confusion	0	1	2	3	2	1
Euphoria	0	0	3	2	2	0
Incoordination	1	0	2	2	2	0
Thinking abnormal†	1	0	1	3	2	0
Tremor	1	1	1	2	1	0
Abnormal gait	1	0	1	3	1	0
Amnesia	3	1	0	2	1	0
Nervousness	0	1	1	1	1	0
Respiratory system						
Dyspnea	3	0	2	2	2	1
Special senses						
Blurry vision‡	3	1	3	6	4	2
Abnormal vision	1	0	1	1	1	0

***PGB: pregabalin**
***Thinking abnormal primarily consists of events related to difficulty with concentration/attention but also includes events related to cognition and language problems and slowed thinking.**
***Investigator term; summary level term is amblyopic**
Overdose
Signs, Symptoms and Laboratory Findings of Acute over dosage in Humans
There is limited experience with overdose of pregabalin. The highest reported accidental overdose of pregabalin during the clinical development program was 8000 mg, and there were no notable clinical consequences. In clinical studies, some patients took as much as 2400 mg/day. The types of adverse events experienced by patients exposed to higher doses (≥900 mg) were not clinically different from those of patients administered recommended doses of pregabalin.
Treatment or Management of Overdose
There is no specific antidote for overdose with pregabalin. If indicated, elimination of unabsorbed drug may be attempted by emesis or gastric lavage; usual precautions should be observed to maintain the airway. General supportive care of the patient is indicated including monitoring of vital signs and observation of the clinical status of the patient.
Special precautions for storage: Store below 30°C in the original package in order to protect from moisture.

Nature and contents of container: Alu/Alu Blister of 10 Capsules, 3 such Alu/Alu blisters packed in a carton.
Caution: Foods, Drugs, Devices and Cosmetics Act Prohibits Dispensing Without Prescription.

For suspected adverse drug reaction report to the FDA: www.fda.gov.ph
Seek medical attention immediately at the first sign of any adverse drug reaction

Mfg.Lic.No.: TN00002269
Shelf Life: 24 Months

Store at temperatures not exceeding 30°C.
Protect from sunlight and moisture.
Keep out of reach of children.

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